

Application No. 09/914,708

Reply to Office Action

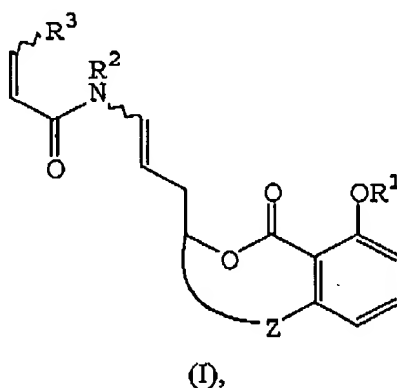
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## AMENDMENTS TO THE CLAIMS

JUL 03 2007

This listing of claims replaces all prior versions, and listings, of claims in the application.

1. (Currently Amended) A method of treating a condition treatable by the inhibition of vacuolar-type (H<sup>+</sup>)-ATPase, said method comprising administering to a patient an amount effective to inhibit vacuolar-type (H<sup>+</sup>)-ATPase of at least one compound of the formula:



wherein

R<sup>1</sup> and R<sup>2</sup> are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, R<sup>6</sup>CH<sub>2</sub>-, R<sup>6</sup>CO-, or R<sup>6</sup>SO<sub>2</sub>-,

wherein R<sup>6</sup> is H, a straight-chain or branched saturated or unsaturated alkyl, or an aryl;

R<sup>3</sup> is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, an oxime, or an oxime methyl ether;

the aromatic ring of formula (I) is unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano;

the saturated alkyl, unsaturated alkyl and aryl substituents defined in R<sup>1</sup>-R<sup>3</sup> and any one or more of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, or R<sup>6</sup> are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; and

Z is a contiguous linker comprising a chain of 7-10 atoms which, together with the five atoms beginning with the carbon of the aromatic ring of formula (I) in meta-relationship

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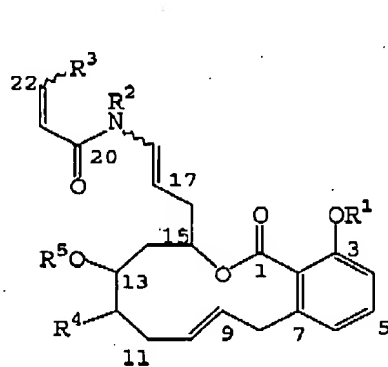
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with OR<sup>1</sup> and ending with the carbon directly attached to the alkyl oxygen of the lactone of formula (I), said carbons being covalently bonded to either end of linker Z, integrally form a 12-15 membered ring;

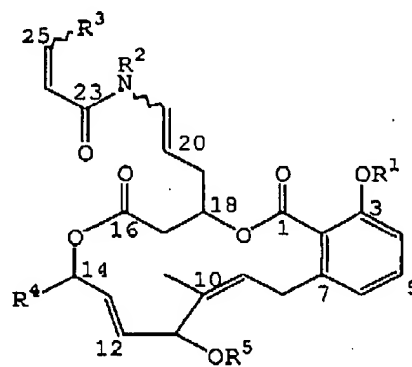
or a pharmaceutically acceptable salt, an ester, or a prodrug thereof, wherein the condition is ~~selected from the group consisting of urinary acidification, bone resorption, osteoporosis, fertility, angiogenesis, glaucoma, and Alzheimer's disease.~~

2. (Canceled)

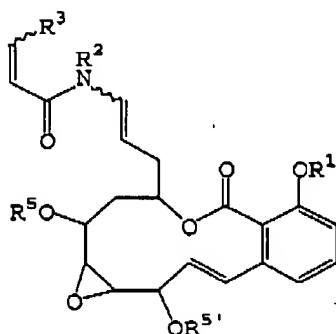
3. (Currently Amended) The method of claim 1, wherein said compound is selected from the group consisting of:



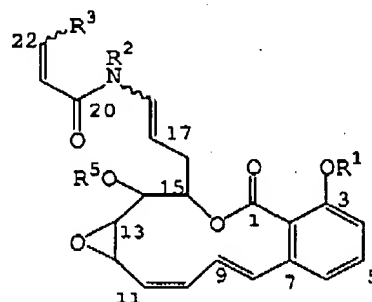
(IA),



(IB),



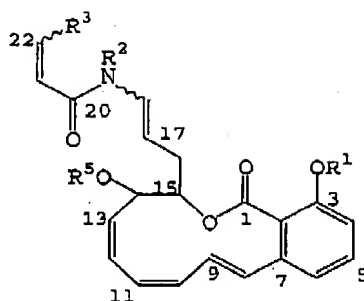
(IC),



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and (IE),

wherein

$R^1$  and  $R^2$  are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl,  $R^6CH_2-$ ,  $R^6CO-$ , or  $R^6SO_2-$ , wherein  $R^6$  is H, a straight-chain or branched saturated or unsaturated alkyl, or an aryl;

$R^3$  is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, an oxime, or an oxime methyl ether;

$R^4$  is H, an alkyl, or  $R^7CH_2-$ , wherein  $R^7$  is  $R^6O-$ ,  $R^6CO_2-$ , or  $R^6SO_3-$ ;

$R^5$  and  $R^{5'}$  are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, a glycoside,  $R^6CH_2-$ ,  $R^6CO-$ , or  $R^6SO_2-$ ;

the saturated alkyl, unsaturated alkyl and aryl defined in  $R^1$ - $R^3$ , any one or more of  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^{5'}$  and or  $R^6$ , and the alkyl defined in  $R^4$ , are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; and

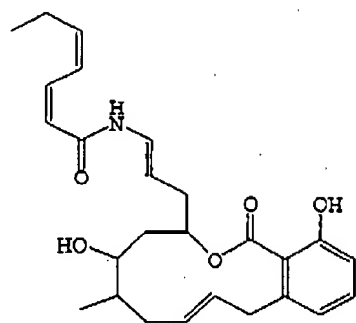
the aromatic ring of formula (I) is unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano;

or a pharmaceutically acceptable salt, an ester, or a prodrug thereof.

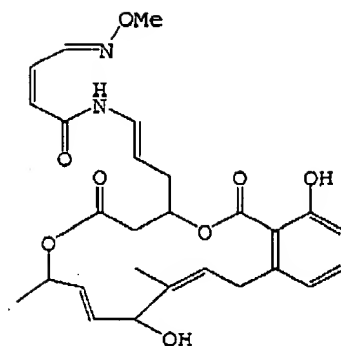
4. (Previously Presented) The method of claim 3, wherein said compound is selected from the group consisting of:

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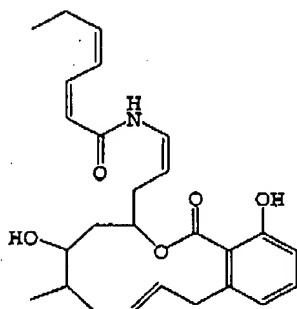
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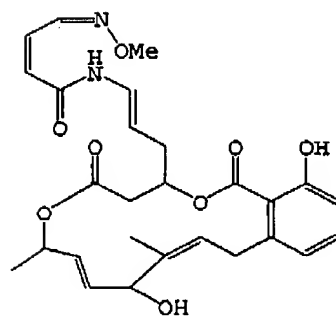
salicylihalamide A,



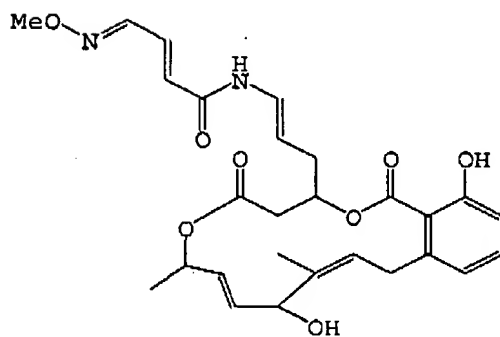
lobatamide A,



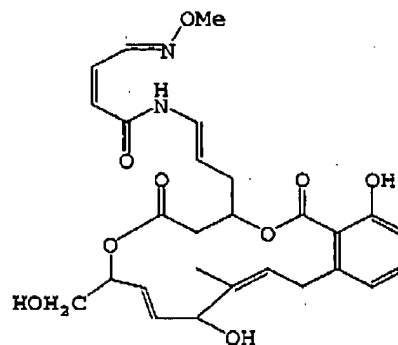
salicylihalamide B,



lobatamide B,



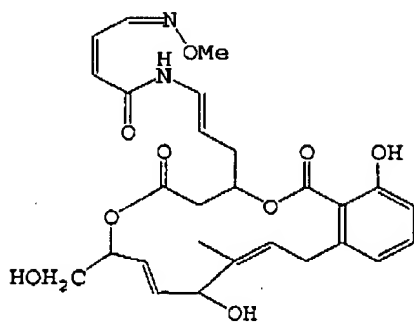
lobatamide C,



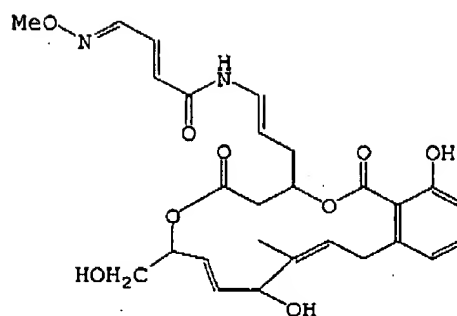
lobatamide D,

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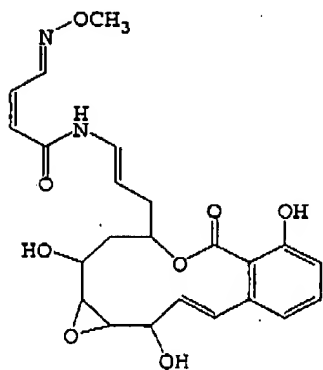
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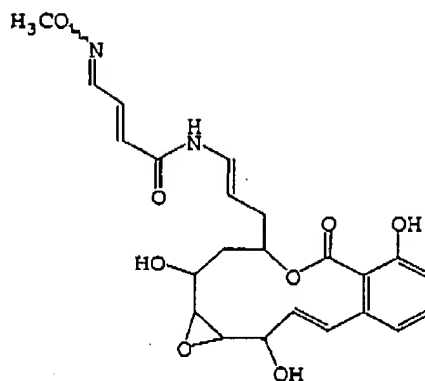
lobatamide E,



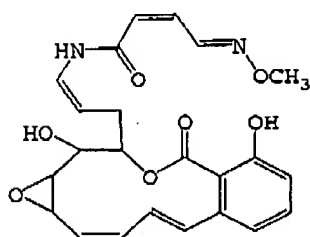
lobatamide F,



CJ-12,950,

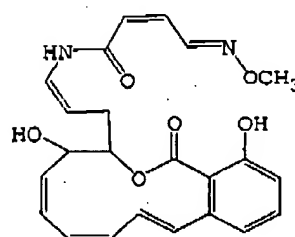


CJ-13,357,



oximidine 1,

and



oximidine 2;

or a pharmaceutically acceptable salt, an ester, or a prodrug thereof.

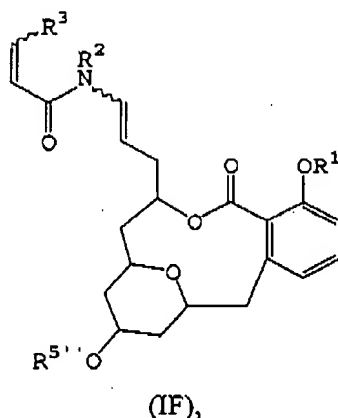
5. (Canceled)

6. (Currently Amended) A method of treating a condition treatable by the inhibition of vacuolar-type (H<sup>+</sup>)-ATPase, said method comprising administering to a patient

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an amount effective to inhibit vacuolar-type (H<sup>+</sup>)-ATPase of at least one compound of the formula:



wherein

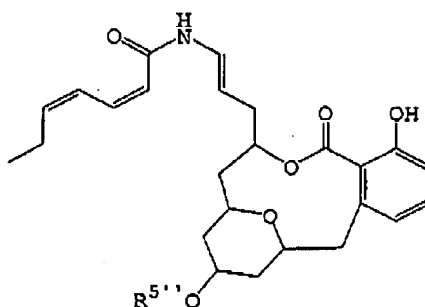
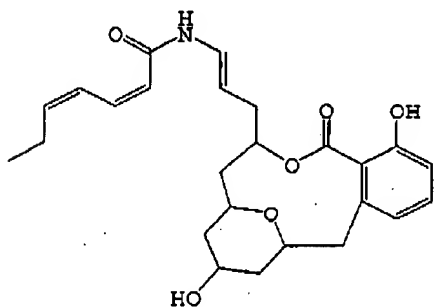
R<sup>1</sup>-R<sup>3</sup> are as defined in claim 1 and

R<sup>5''</sup> is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, a glycoside, R<sup>6</sup>CH<sub>2</sub>-, R<sup>6</sup>CO-, or R<sup>6</sup>SO<sub>2</sub>-, wherein R<sup>6</sup> is as defined in claim 1 and

the saturated alkyl, unsaturated alkyl and aryl defined in R<sup>5''</sup> are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano,

wherein the condition is ~~selected from the group consisting of urinary acidification, bone resorption, osteoporosis, fertility, angiogenesis, glaucoma, and Alzheimer's disease.~~

7. (Previously Presented) The method of claim 6, wherein said compound is selected from the group consisting of:



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apicularen A and apicularen B,

wherein R<sup>5''</sup> is N-acetyl- $\beta$ -D-glucosamine.

8. (Previously Presented) The method of claim 1, which further comprises co-administering to a patient in need thereof a therapeutically effective amount of at least one additional compound other than a compound defined in claim 1.

9. (Previously Presented) The method of claim 8, wherein said additional compound is selected from the group consisting of bafilomycins and concanamycins.

10. (Previously Presented) The method of claim 9, wherein said additional compound is concanamycin A.

11. (Previously Presented) The method of claim 9, wherein said additional compound is bafilomycin A<sub>1</sub>.

12. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H<sup>+</sup>)-ATPase inhibiting-effective amount is effective to inhibit intra-organellar acidification of intracellular organelles.

13. (Canceled)

14. (Canceled)

15. (Currently Amended) The method of claim ~~14~~ 1, wherein said vacuolar-type (H<sup>+</sup>)-ATPase inhibiting-effective amount is effective to treat osteoporosis.

16.-33. (Canceled)